

VBI VERY BRIEF INTERVENTIONS

Very brief interventions to promote physical
activity in primary care

TRIAL PROTOCOL

Version number:5
Version date: 07/09/2015

The VBI trial: A randomised controlled trial of the effectiveness and cost-effectiveness of a very brief intervention to increase physical activity in adults attending NHS Health Checks



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Protocol Version Control

Version number	Version Date	Protocol approvals and dates (e.g. REC etc.)	Supersedes approved version number/date
2.0	01/04/2014	For Insurance/Sponsorship and REC application	Not applicable
3.0		To address concerns raised by the REC	2.0
4.0	17/12/2014	To amend how the follow up questionnaires will be sent to study participants	3.0
5.0	07/09/2015	Efficacy now reads effectiveness. Minor changes to wording and research team members. A piece from the statistical analysis is no longer relevant. Extra clarity provided in the following areas; exclusion criteria and process measures. 2 additional procedures added: Obtaining information on any referrals to health trainers and/or exercise referral programmes. GP to send reminder/thank you letter to retrieve outstanding accelerometers.	4.0

Trial Contact Details

Chief Investigator: Professor Stephen Sutton
 Professor of Behavioural Science
 The Primary Care Unit
 Dept. Public Health & Primary Care
 Institute of Public Health, Forvie Site
 University of Cambridge School of Clinical Medicine
 Box 113 Cambridge Biomedical Campus
 Cambridge. CB2 0SR
Email: srs34@medschl.cam.ac.uk
Tel: 01223 330594
Unit fax: 01223 762515

Principal Investigator: Dr Wendy Hardeman
 Senior Research Associate in Behavioural Science
 The Primary Care Unit
 Dept. Public Health & Primary Care
 Institute of Public Health, Forvie Site
 University of Cambridge School of Clinical Medicine
 Box 113 Cambridge Biomedical Campus
 Cambridge. CB2 0SR
Email: wh207@medschl.cam.ac.uk
Tel: 01223 762513

Trial Co-ordinator: Ms Joanna Mitchell
 Research Associate/Trial Coordinator
 The Primary Care Unit
 Dept. Public Health & Primary Care
 Institute of Public Health, Forvie Site
 University of Cambridge School of Clinical Medicine
 Box 113 Cambridge Biomedical Campus
 Cambridge. CB2 0SR
Email: jm294@medschl.cam.ac.uk
Tel: 01223 761760

Definitions

CRF	Case Report Form(s)
GCP	Good Clinical Practice
GP	General Practitioner
HCA	Healthcare Assistant
ISRCTN	International Standard Randomised Controlled Trial Number
NIHR	National Institute for Health Research
NHS	National Health Service
NIHR CRN	National Institute for Health Research Clinical Research Network
NICE	National Institute for Health and Care Excellence
PCF	Participant Consent Form
PCRN	Primary Care Research Network
PCU	Primary Care Unit
PIS	Participant Information Sheet
PN	Practice Nurse
PPI	Patient and Public Involvement
RCT	Randomised Controlled Trial
R&D	Research and Development
REC	Research Ethics Committee
UKCRN	United Kingdom Clinical Research Network
VBI	Very Brief Interventions

Trial Synopsis Table

Trial short title	Very brief interventions (VBI): A randomised controlled trial
Trial full (scientific) title	The VBI Trial: A randomised controlled trial of the effectiveness and cost-effectiveness of a very brief intervention to increase physical activity in adults attending NHS Health Checks
Public title	The VBI Trial
Chief Investigator	Professor Stephen Sutton
Principal Investigator	Dr. Wendy Hardeman
Investigator's employing institution	University of Cambridge
Sponsor	University of Cambridge
Funder	National Institute for Health Research
NIHR Programme Grant Ref #	RP-PG-0608-10079
ISRCTN	ISRCTN72691150
UKCRN ID	16952
Trial duration	18 months
Setting	Primary Care – 23 General Practice surgeries in the East of England.
Participants	Participants eligible for an NHS Health Check, aged 40-74.
Sample size	1140
Treatment groups	Intervention and control
Primary outcome measure	Physical activity, as measured by accelerometer counts per day.
Secondary outcome measure(s)	Self-reported physical activity, as measured by the Recent Physical Activity Questionnaire; Cost of intervention.
Follow-up	3 months post intervention.
Analysis	ANCOVA to test for an intervention effect using an intention to treat approach

The VBI trial: A randomised controlled trial of the effectiveness and cost-effectiveness of a very brief intervention to increase physical activity in adults attending NHS Health Checks

Summary

Physical activity can delay or prevent the onset of chronic diseases such as vascular disease, which includes heart disease, stroke, diabetes and kidney disease. However the majority of adults in England do not meet the government recommendation of at least 30 minutes per day of moderate-intensity activity on at least five days per week. The Primary Care GP practices under the umbrella of Clinical Commissioning Groups are conducting Health Checks, in which everyone between 40 and 74 years is invited for an assessment of their 10 year risk of developing vascular disease and offered appropriate management of risk. The Health Checks are therefore an ideal opportunity to deliver brief interventions to promote physical activity to large numbers of people. The present trial forms part of a larger programme of on-going and inter-related research, funded by an NIHR Programme Grant, which aims to develop and evaluate very brief interventions to increase physical activity in primary care.

In this trial we will test a pedometer-based intervention identified from our pilot trial and other sources of evidence as the most promising very brief intervention for promoting physical activity in adults attending an NHS Health Check. We aim to recruit 1140 participants in 23 practices in the East of England. The intervention will be delivered by practice nurses (PN) or healthcare assistants (HCA) at the end of the Health Check. The primary outcome measure will be an objective measure of physical activity obtained using an accelerometer (ActiGraph) worn around the hips for seven days at three months post intervention. The consultations will be monitored for fidelity and length of delivery. An economic evaluation will be conducted alongside the trial.

Non-responders will be identified from this trial and be invited to take part in “Reasons for Non-Participation in Physical Activity Interventions: A Mixed Methods Study” REC reference: 13/LO/1163.

Trial Objective

The objective of this trial is to obtain estimates of the effectiveness and cost-effectiveness of a very brief pedometer-based intervention to promote physical activity in adults aged 40-74 years attending an NHS Health Check.

Background to the VBI trial

Vascular disease, which includes coronary heart disease, stroke, diabetes and kidney disease, affects more than four million people in England, causes one out of three deaths and one out of five hospital admissions [1]. Unhealthy behaviours such as a sedentary lifestyle are important risk factors for these diseases [1], and lack of physical activity is the fourth most important risk factor worldwide [1]. In addition, physical inactivity in the UK represents a direct and indirect cost to society of £8.2 billion [2]. The current recommendation for adults is that they should aim to take 30 minutes of moderate intensity physical activity, e.g., brisk walking, on at least five days per week. The 2008 Health Survey for England [3] found that only 44% of men and 33% of women between 35 and 44 years met this recommendation. This fell to 20% of men and 18% of women aged 65 to 74 years. These figures are based on self-reports of physical activity, and people tend to overestimate how active they are. When activity was measured objectively with an accelerometer, only 6% of men and 4% of women met the recommendation. Despite the hoped for Olympics Legacy Effect, initial results from the 2012 Health Survey for England [3] indicate that these figures have remained stable.

There are several systematic reviews of the effects of interventions to promote physical activity. A narrative review by NICE in 2006 concluded that brief advice by primary care practitioners showed promise, but there was uncertainty about the most effective approaches among groups at higher risk of chronic disease [4]. The US Preventative Services Task Force stated that it was not clear whether physical activity counselling in primary care is effective and they recommended more research on this topic [5]. Published trials of physical activity interventions suffer from a number of limitations. The interventions are often not described in sufficient detail to identify the 'active ingredients' and to enable others to replicate the intervention [6, 7], and many trials use only self-report measures of physical activity, which may lack validity. The recent NICE report [8] focuses on brief physical activity advice and acknowledges that brief advice has some impact on physical activity levels; however, there is insufficient evidence to make recommendations about the differential impact of brief advice based on duration of delivery, content or by who delivers it. However, health professionals have been identified as having the potential to be powerful mediators for physical activity promotion [9], and the US Preventive Service Task Force more recently state [10] that behavioural interventions may be more effective when undertaken in the context of broader public health interventions. However, for some health professionals, time (e.g. limited consultation time) and a lack of perceived effectiveness (i.e. doubt about whether the intervention will lead to an increase in physical activity) are seen as key barriers to the success of such interventions [9].

The NHS is currently conducting Health Checks which are offered to all adults between 40 and 74 years. Health Checks include an assessment of a person's risk of vascular disease and advice and treatment tailored to the person's individual need [1]. Public Health England [PHE] fully supports the NHS Health Check programme [11] and works with local authorities to improve the uptake of this scheme. The Health Checks therefore offer an ideal opportunity to deliver very brief physical activity interventions to a large proportion of the population. Very brief physical activity interventions (lasting no more than 5 minutes) should be relatively easy and inexpensive to implement on a large scale, and a small effect on physical activity level could translate into a significant public health benefit.

We have developed several very brief interventions and have conducted pilot studies, including a pilot trial (12-EE-0200), to assess their feasibility, acceptability and potential effectiveness when delivered by a practice nurse or healthcare assistant as part of an NHS Health Check. This randomised controlled trial (RCT) will test the effectiveness of the intervention judged to be the most promising (i.e. it can be delivered within 5 minutes and is acceptable, feasible and potentially effective) in promoting an increase in physical activity, namely a pedometer-based intervention.

The comparator will be a routine Health Check (which includes basic lifestyle advice). The trial will thus estimate the incremental effectiveness and cost effectiveness of adding a very brief pedometer-based physical activity intervention to the routine Health Check.

Design and methods

Design

The design is a two parallel group randomised controlled trial (RCT) with 1:1 individual allocation comparing usual care (standard Health Check) with usual care plus a very brief pedometer-based intervention. Follow-up will be three months post-intervention using an objective measure of physical activity (accelerometer counts).

Design decisions were informed by our pilot trial and other considerations. We considered using a clustered design (with practice as the unit of randomisation) but it is likely that this would require a larger and more expensive trial. Individual randomisation (with patient as the unit of randomisation) is more efficient but there is a greater risk of contamination. More specifically, it is possible that the intervention deliverers (practice nurses and healthcare assistants) may inadvertently use elements of the intervention with control participants, thus diluting the intervention effect. However, our previous experience of trials of behavioural interventions delivered by primary care practitioners suggests that they can be trained to switch easily between delivering intervention and control to successive patients without contamination.

A second key design decision was not to assess the primary outcome of physical activity at baseline. It would be logistically difficult to obtain 7 days of accelerometer data from each participant before they attend their Health Check. More importantly, the present trial is assessing the effect of a very brief intervention, and wearing an accelerometer for 7 days at baseline may itself act as an intervention. We therefore prefer the simpler option of assessing the primary outcome only at follow up. The relatively large sample size and individual randomisation mean that the two trial groups are likely to be similar at baseline (and we will be able to check comparability with respect to demographic variables). We will not be able to assess individual change in physical activity but the design should yield a robust estimate of the difference in mean physical activity between trial groups at follow up, which is the key parameter of interest.

Participants

Inclusion Criteria

Participants will be adults aged 40-74 who are eligible to be invited for a NHS Health Check and who are able to give consent for participation in the trial. Patients are eligible for a NHS Health Check if they have not already been diagnosed with vascular disease such as type 2 diabetes, heart disease, kidney disease and peripheral vascular disease and who are not already on a separate care pathway for identifiable risks such as raised blood pressure. Non-English speaking patients may bring with them an interpreter to aid with the understanding of the Health Check and the trial or (if it is available) use the translator facility provided by the GP Surgery. It will be made clear however that for a patient to be included in the trial they must be able to complete the follow up measurements 3 months after the Health Check for which an interpreter may still be required. Any patient unable to fulfil this criterion is still eligible for the NHS Health Check.

Exclusion Criteria

The GP practice will exclude patients they consider unsuitable for the trial (i.e. any patient where receiving an invitation will cause unnecessary stress due to mental health issues or a diagnosis of terminal illness for example).

Written guidance will be given to GP practices to aid the process of drawing up a list of patients eligible for a NHS Health Check.

Practice recruitment and training

The research team, in collaboration with the East of England Primary Care Network (PCRN) will approach GP practices to ascertain their interest in taking part in the trial. Potential practices will be subsequently contacted via letter/email/telephone and personal approaches (i.e. meetings with practice teams at a mutually convenient time to discuss the trial) to solicit their participation. In order to recruit 1140 participants and to reduce the burden for each GP practice we will need to recruit 23 GP practices in total. For interested practices, staff responsible for delivering the Health Checks will be provided with an information sheet giving an overview of the trial and what their participation would involve.

In order to secure high quality research data, participating practice nurses and healthcare assistants will receive training on how to deliver the very brief intervention and the importance of collecting and recording accurate, explicit and complete data for all participants. Training will also include other research skills including the taking of informed consent and the issue of confidentiality within a research setting. All nurses and HCAs responsible for delivering the Health Check will be trained in how to follow the research and intervention protocol, to complete case report forms and to deliver the intervention within the consultation. We anticipate, on the basis of our pilot work (12-EE-0200), that this training could be done in a two hour session at the surgery. Follow-up training and on-going support will be available on a flexible basis, depending on individual practice nurse/HCA's needs.

Nurses and HCAs will also be made aware of the possible sources of bias when delivering the Health Checks, in particular the need to follow the protocol closely when delivering the intervention and to avoid giving extra advice/support on physical activity during the control consultations. Fidelity will be monitored by recording a sample of both control and intervention consultations at intervals throughout the trial.

Participant recruitment and consent

The NHS Health Check is available to everyone aged between 40 and 74 years who has not already been diagnosed with vascular disease and who is not already on a separate care pathway for identified risks (e.g. raised blood pressure).

In each practice, a random sample of patients will be drawn from the list of those eligible for NHS Health Checks. Practice staff will export, to a secure USB data pen, an unidentifiable ID number for all patients eligible for the Health Check. The trial statistician will then randomly select 250 patients to receive a trial invitation, and this list of ID numbers will be transferred to the practice. (The proposed procedure may need to be adapted for different practices, depending on the computer system they use, the numbers of Health Checks they carry out per week, the numbers of eligible patients and the response rates achieved.)

Practices can choose to send out study information at the same time as sending out the invitation for a NHS Health Check **OR** invite patients from the randomly selected list for a NHS Health Check

and then once the appointment has been booked send out study information packs prior to the Health Check.

It is desirable that patients are given enough time to consider the information before deciding whether to take part in the trial, and all GP surgeries initially will use the preferred method of recruitment, but it is also important that the uptake of Health Checks is not compromised. In our recent pilot trial (12-EE-0200), surgeries that were having difficulties with recruitment have used an alternative strategy. One surgery in particular noted that take up of the Health Check was reduced when patients received study information at the same time as a NHS Health Check invitation. The Cambridge Central REC gave approval for patients to instead be given a study information sheet in the waiting room and the nurse or healthcare assistant to answer any questions that arose at the start of the consultation. Using this opportunistic method, take up for the NHS Health Check increased significantly thus recruitment to the study also increased as a result. Therefore GP surgeries experiencing a significant reduction in the uptake of Health Checks in this study may also opt to use this alternative method of recruitment. A spreadsheet will be kept at each surgery to record the date the participant was sent the information sheet and the date of the Health Check to ensure adequate time has lapsed between receiving the information and giving informed consent. Where participants have received the information sheet in the waiting room the time of receipt of the information sheet will be logged on the CRF.

Study information packs will include an invitation letter, a participant information sheet [PIS], and a sample participant consent form [PCF]. Assuming a conservative 20% response rate based on our previous work, each practice will contact up to 250 eligible participants. Reminders will be sent after 2-3 weeks for non-responders. In 5 GP practices in Cambridgeshire a 2nd reminder including an opt-out slip will be sent after a further 2 weeks. This slip enables the patient to opt-out of receiving any further communication from the study team, more specifically from receiving information from the non-responder study (REC reference: 13/LO/1163).

At the beginning of the Health Check the participant will sign a consent form; the nurse or healthcare assistant will ensure that consent is freely given by the patient and that they understand all aspects of study involvement.

Interventions

Three very brief interventions were evaluated in the pilot trial (12-EE-0200). Of these, the Pedometer Intervention was selected as the 'best-bet' intervention to be evaluated in the present trial. This decision was made using a systematic and documented procedure in which multiple sources of evidence were used to evaluate each intervention against the following pre-specified criteria: potential effectiveness, feasibility, acceptability and cost.

The Pedometer Intervention will be delivered at the end of the Health Check and consists of the following three components:

Face-to-face discussion in which the practitioner: (i) gives the patient feedback on their current activity; (ii) gives information about the current physical activity recommendations (30minutes of moderate-intensity activity on 5 or more days a week OR 10,000 steps per day); (iii) shows the patient how to wear/use the pedometer and encourages them to use it to monitor the number of steps walked each day; (iv) explains that the Pedometer Booklet gives tips for how to increase daily steps by making small changes; (v) shows the patient the Step Chart and encourages them to use it to set a step goal and record daily steps to monitor whether they reached that goal.

Pedometer & Step Chart: A Yamax Digiwalker SW200 and a printed Step Chart are given to the patient to use as self-monitoring tools.

Pedometer Booklet: containing information on the UK government physical activity recommendations, instructions on how to use the pedometer, and tips for achieving more steps.

In the pilot trial, this intervention was delivered in 5 minutes on average.

Thus, the Intervention Group will receive the ‘usual care’ for NHS Health Check (which includes some basic advice on health and lifestyle) plus the Pedometer Intervention. The Control Group will receive the usual care for NHS Health Check only.

Randomisation

Participants will be randomly allocated within practice nurse/healthcare assistant to either the intervention (i.e. the Health Check plus intervention) or control (i.e. routine Health Check) group. Randomisation to trial group will be carried out by the nurse or healthcare assistant at the beginning of the Health Check using a web-based randomisation tool called Sealed Envelope (<http://www.sealedenvelope.com>). The stratification by practitioner will use blocks of sufficiently small size to provide effective balance across arms.

The practice nurses, HCAs and the participants will not be blind to the intervention condition. However, efforts will be made to reduce the risk of possible bias in assessment of outcome by use of an objective physical activity measure administered independently of the practice team. 10% of Health Checks with and without the intervention will be audio-recorded to ensure fidelity between practice teams and across the surgeries. A randomisation procedure will also be utilised to select the Health Checks to be recorded for fidelity assessment.

Procedure

The nurse or healthcare assistant will obtain informed consent from the patient before beginning the Health Check. Once the participant has given consent, the nurse or HCA will go through the normal procedure of the Health Check with the addition of giving the intervention at the end to intervention participants only. The nurse or HCA will complete a CRF for all participants, and participants will complete a short questionnaire.

It is our experience from the pilot work leading up to this trial (12-EE-0200 and 13/EE/0361) that there is variability in how the NHS Health Check is delivered within and across GP practices. (Therefore in order to individually tailor the incorporation of the VBI into the Health Check and to describe this variation we will audio-record two Health Checks from each practitioner prior to training in the VBI trial procedures. In addition we aim to record a random 10% sample of Health Checks in both trial conditions throughout the duration of the trial to allow us an insight into the effectiveness of training and whether the delivery of the routine Health Check has been altered as a result. Consent will be sought from the participant and the healthcare practitioner for this procedure and the participant’s consent will also be recorded verbally on the recording device at the start of each Health Check. It will be made clear to the participants in the information sheet that if they do not want their Health Check recorded they are under no obligation to do so and they are still eligible to take part in the trial.

Outcome will be assessed 3 months post Health Check. All participants will be sent through the post an accelerometer (a small device about the size of a matchbox) to be worn around the waist for 7 days and a questionnaire that will include questions on recent physical activity, an assessment of what physical activity information was received during the health check (e.g. was there a discussion on PA, did you receive the pedometer?), the use and evaluation of health

services, out of pocket expenses relating to physical activity and any time off work due to ill health (using an adapted version of the Work Productivity and Activity Impairment Questionnaire [12]). Participants will be sent a reminder one week beforehand and invited to arrange with the research team (if needed) a convenient time to receive the accelerometer and complete the questionnaires.

Participants who complete all the follow up measures will be entered into a prize draw. The draw will take place once data collection is complete and 20 participants will each receive a £20 voucher. In the event that participants do not return the accelerometer after repeated attempts to recover it (a 3 month period), the GP practice will send a reminder letter on our behalf.

For all patients participating in the trial we will obtain the 10 year Cardio-vascular Risk scores (calculated from the measures taken during the Health Check). There is an item on the consent form that refers to this. We will also obtain aggregate data on the number of participants referred to a health trainer or exercise referral programme as a result of their health check (i.e. were any of the participants referred to other physical activity programmes as a result of their health check, if so how many and what programmes were they?).

Outcome measures

The **primary outcome** is physical activity at 3-month follow-up, as measured by accelerometer counts per day.

The **secondary outcomes** are: Self-reported physical activity, as measured by the Recent Physical Activity Questionnaire and cost, as measured by the Resource Use Questionnaire.

Process Measures

How the intervention is delivered and the content of the intervention/health check received by each participant will be explored through audio-recordings of a sub-sample of health checks and questionnaire data at follow-up.

Sample size

A trial of 394 followed up per arm is sufficient to detect a 0.2sd (“small”) difference in mean activity between groups (40 accelerometer counts per minute) with 80% power. Allowing for attrition of 30% at follow-up (i.e. 30% of participants not providing sufficient accelerometer data), an initial sample size of 570 per group would give 80% power to detect an effect of this size between the two conditions ($\alpha = 0.05$, 2-sided test).

Observations from our pilot trial (12-EE-0200) suggest that a trial of this size is feasible within the specified resources and timeframe, given the large numbers of people who will be invited for NHS Health Checks, the brevity of the intervention, the remote measurement (done by post), and a 3-month follow-up period. Recruitment to the pilot trial varied depending on the time of year (e.g. flu clinics reduced the time available for Health Checks) but recruitment rate per practice averaged two participants per week. Therefore assuming that each practice recruits two participants a week this would yield about 50 participants per practice over a 6-month period. We would therefore need 23 practices to give the required sample size of 1140.

Statistical analysis

We will use analysis of covariance to test for intervention effects on continuous outcomes and quantify these with differences in means and 95% confidence intervals, adjusting for any baseline randomisation stratifiers. Logistic regression will be used correspondingly for binary outcomes. An intention to treat approach will be used, supported by a per protocol analysis for the primary outcome analysis. Missing data in the primary outcome will be handled within a sensitivity analysis considering optimistic and pessimistic scenarios for the intervention effect size in those with missing data and incorporating baseline predictors of primary outcome missing status that are differential by arm. Pre-specified subgroup variables will be examined in relation to the primary outcome and will involve an initial test of differential intervention effect across the subgroup variable before summarising randomised effect within subgroup categories. They will include: baseline cardiovascular risk, gender; age ethnic group; educational qualifications; employment status; urban vs. rural; individual-level deprivation score; and area-level deprivation score (IMD 2007, derived from postcode). For a continuous moderator such as CVD risk, the intervention effect observed in the highest tertile of the moderator will be estimated with a 95% confidence interval having an informative width of +/- 25 thousand activity counts per day. All tests will be two-sided and assessed at the 5% level of significance. Further details of the statistical methods will be described in a statistical analysis plan.

A within-trial economic evaluation will be performed estimating the incremental cost per incremental minute of brisk walking gained (or equivalent, converted from accelerometer counts). The analysis will be conducted from the perspective of the NHS and society. NHS costs will comprise the cost of providing the intervention (e.g. pedometer and associated materials purchased plus GP, nurse or healthcare assistant time to deliver the intervention), subsequent primary and secondary care activity and prescribed medications. Societal costs will include NHS costs plus patient out of pocket expenditure on physical activity (such as gym memberships), and lost productivity due to any time off work due to ill health.

Current guidelines in the conduct and reporting of economic evaluations will be followed [13-15]. Analysis of uncertainty will comprise estimation of 95% confidence intervals around incremental costs and outcomes, and construction of the cost-effectiveness acceptability curves.

In addition to the within-trial analysis, results will be combined with prior data on the costs and effects of the chosen intervention, and a previously developed model will be updated with the new evidence to predict the longer term costs and outcomes associated with the intervention and comparator(s). This will yield a revised estimate of the incremental cost per QALY gained (as well as other outcomes). The revised decision uncertainty will be reported as an updated cost-effectiveness acceptability curve.

We will use a coding framework to analyse the voice recordings for fidelity once recruitment is complete. Features of the Health Check and the Intervention will be coded on a Yes-present/No-absent basis to provide a descriptive analysis of the Health Check and the VBI across and between GP practices.

Duration of trial

Overall recruitment is anticipated to take 15 months between June 2014 and September 2015. Excluding training and set up meetings the duration of participation for each GP surgery is likely to be approximately 6 months based on each recruiting 2 participants a week (this figure is feasible based on the evidence from the pilot study (12-EE-0200)). The duration of individual participant

involvement is expected to be between 12 and 14 weeks from the Health Check to the end of the follow up period (3 months post intervention).

Participant withdrawal

Participants are free to withdraw from the trial at any time. This is made clear to participants in the PIS and the PCF. Furthermore, if the patient does withdraw from the trial (at any point), it is made clear to them that they are still eligible to attend a free NHS Health Check (even if they are no longer part of the trial).

Archiving

Personal data will be retained until there are no further results to disseminate by means of newsletters etc. Sensitive personal data collected to answer specific research questions will have all identifiable markers removed and archived in accordance with Good Clinical Practice along with all other research data and essential documents for 20 years

Site files will be retained at each site for 2 years after completion of the study.

Ethical considerations

Informed Consent

Participants will receive an information sheet (PIS) and a sample consent form (PCF) prior to their Health Check. They will have the opportunity to ask questions before deciding whether to take part. The information sheet will outline that the trial is entirely voluntary and if they do not want to participate then they are still eligible for the Health Check. The PIS will also contain contact details of the trial coordinator who can be contacted if the participant has any questions about the trial.

When potential participants are sent an invitation pack by post they may take up to two weeks to decide if they wish to take part. After 2 weeks, they will be sent a reminder letter. If they do not respond after a further 2 weeks it will be assumed that they do not wish to take part in the trial.

Written consent will be obtained at the start of the Health Check and verbal consent will also be sought on the occasions when the Health Check is being recorded for quality assurance purposes. Consent will be recorded on the audio device.

The process of soliciting informed consent from all participants will ensure that they understand the purpose of the research and what it involves (including any risks or burdens). Potential participants must demonstrate their understanding of the trial and the nurse or healthcare assistants must be confident of this before enrolling the patient into the trial. Full Informed Consent training will be provided by the research team. It will be made clear to patients that if they are unable or do not wish to take part in the research it will not affect the care they receive and they are still eligible for the NHS Health Check.

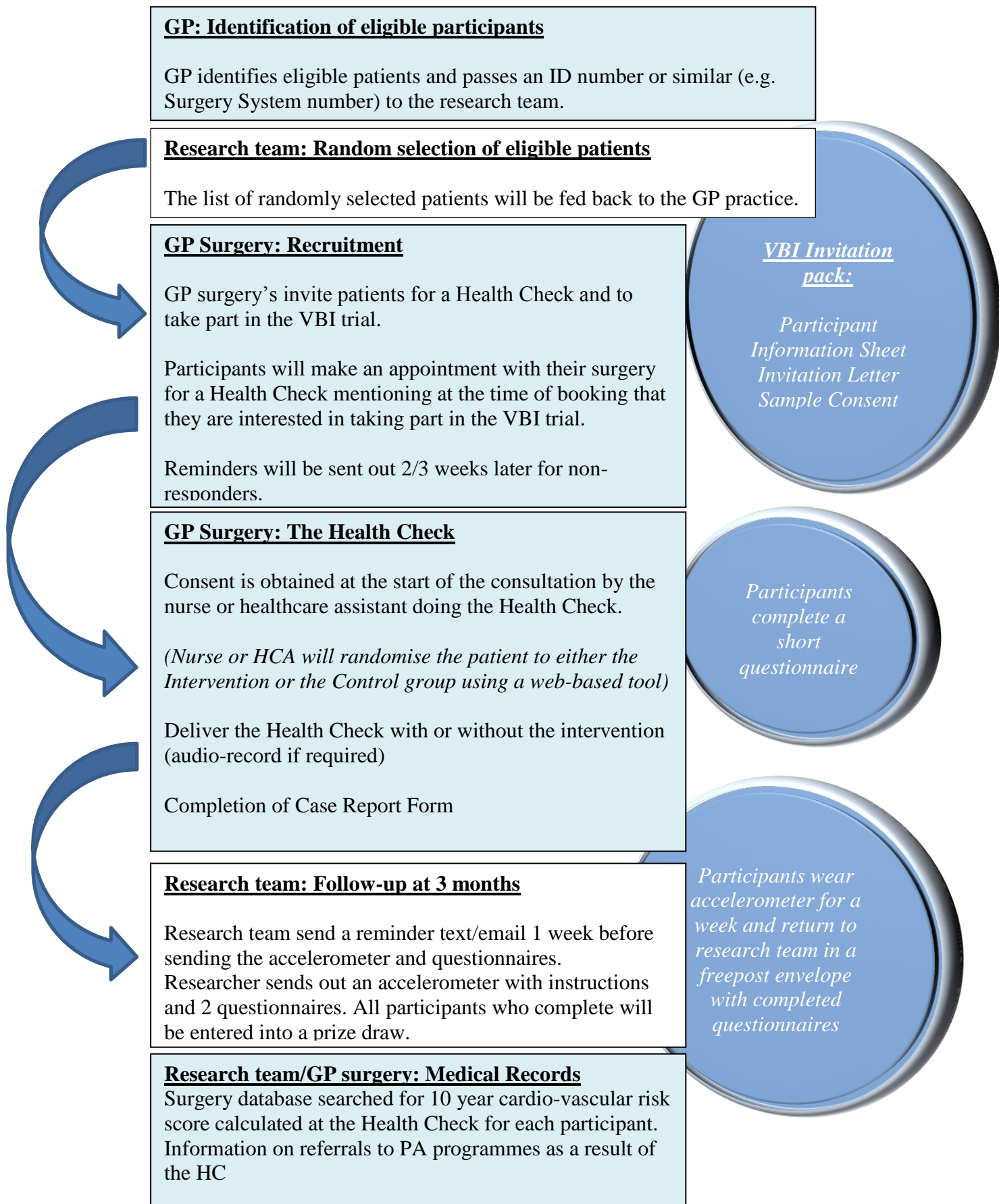
Potential Risks and/or Burdens for Participants

This trial recruits participants who are eligible to receive a free NHS Health Check at their local general practice. The present trial is delivered within the NHS Health Check consultation; therefore any burdens and risks to the participant will be minimal (an extra 5 minutes added to the length of the consultation). However, some participants may find some of the questions intrusive; the reasons for asking the questions are explained in the PIS. Additional burdens outside of the Health Check would be the time and inconvenience it takes to complete two questionnaires and wear an accelerometer for one week 3 months after the Health Check. Even if participants do not wish to take part in the research trial, they are still eligible to attend the NHS Health Check and it will not affect the care they receive (and this will be made clear to them in the PIS and PCF).

Overall, potential risks to participants, researchers and practice staff in this trial will be negligible. The interventions used in the trial are behaviour change interventions that aim to encourage moderate physical activity such as brisk walking which carries a very low risk of injury. Our previous trials of more intensive physical activity interventions (e.g., ProActive and *ADDITION-Plus*) have measured adverse effects and found none [16, 17]. Furthermore, NHS Health Checks contain elements of risk management (i.e., routine advice [1]); therefore this trial does not impose additional risks to patients that go beyond usual care.

The potential risk of a breach of confidentiality is minimised by ensuring that only the research team will have access to the data collected (with two exceptions: independent auditors may require access to the data and the MRC Epidemiology Unit will have access to the anonymised objective physical activity data for analysis purposes). All participants will be assigned an ID number that is linked to the research data (rather than their name). Furthermore, the PCU is fully GCP compliant and all data are handled according to regulatory standards with password protection, locked filing cabinets, and storage of electronic data in encrypted volumes on a University server.

Event schedule for the Trial



Trial Management and Governance Arrangements

Research Team

Chief Investigator:	Professor Stephen Sutton	University of Cambridge
Principal Investigator	Dr. Wendy Hardeman	University of Cambridge
Research team:	Ms Jo Mitchell – Trial Co-ordinator	University of Cambridge
	Dr. Sally Pears - Intervention Developer	University of Cambridge
	Miranda Van Emmenis– Research Assistant	University of Cambridge
	Florence Theil – Research Assistant	University of Cambridge
Trial Collaborators:	Practice Nurses (or HCAs)	GP Practices
	Mr James Brimicombe	University of Cambridge
	Professor Simon Griffin	University of Cambridge
	Professor Ann-Louise Kinmonth	University of Cambridge
	Professor Toby Prevost	Kings College London
	Mr Vijay Singh GC	University of East Anglia
	Prof Marc Suhrcke	University of East Anglia
	Dr Ed Wilson	University of Cambridge

The day to day management of the trial will be performed by the Research Team based at the Primary Care Unit, Institute of Public Health, University Forvie Site, Cambridge. The CI, PI and Study Team will hold monthly Trial Review Meetings in order to review on-going progress of the trial and any amendments required.

Sponsor

The Department of Health’s Research Governance Framework for Health & Social Care (2nd Edition, 2005), states that “for any research that takes place in the context of the NHS or social

care services in England there must be a sponsor.” The ‘Sponsor’ is defined as the “Individual, organisation or group taking on responsibility for securing the arrangements to initiate, manage and finance a trial.

The **University of Cambridge** will act as Sponsor for the VBI trial.

Trial Funding and NHS Costs

Research Costs

The research costs for the trial are funded through a programme grant awarded by the National Institute for Health Research (NIHR): **Reference: RP-PG-0608-10079**

NHS Service Support Costs

NHS Service Support Costs include the additional NHS patient-care costs associated with the research, which would end once the R&D activity in question had stopped, even if the patient care service involved continued to be provided (Department of Health, Attributing revenue costs of externally funded non-commercial research in the NHS (ARCO) December 2005).

Additional NHS Service Support will therefore be sought from the relevant NHS Trust(s), Comprehensive Local Research Network(s) and/or East of England Primary Care Research Network, as appropriate.

The National Institute for Health Research (NIHR) Clinical Research Network (CRN), which is the English component of the UK Clinical Research Network (UKCRN), is the route for access to funding for NHS Service Support Costs in England.

Adoption of the VBI Trial onto the UKCRN Clinical Research Portfolio

The UKCRN Clinical Research Portfolio comprises the NIHR Portfolio in England, and the corresponding portfolios of Northern Ireland, Scotland and Wales. As the VBI trial is funded by the NIHR, the trial is automatically eligible for inclusion in the NIHR CRN Portfolio of studies and thus to NIHR CRN support. Studies are assigned to Topic(s) within the NIHR CRN Portfolio and the VBI trial is part of the Primary Care Research Network (PCRN) Topic.

The research team will provide information on the number of participants recruited to the NIHR CRN accruals database, which is a condition of NIHR CRN support for the trial.

Insurance/Indemnity

The University of Cambridge insurance office has been consulted to ensure appropriate insurance/indemnity arrangements are in place to meet the potential legal liability of the Sponsor, investigators/collaborators arising from harm to participants in the design, management and conduct of the research (**Ref: B0823Q31000177**).

Participants are NHS patients, therefore indemnity is provided through NHS schemes or through professional indemnity. GP Practices must check with their providers of insurance that participation in the research is covered for negligent harm.

Adverse Incidents Reporting

As the VBI trial is not a 'clinical trial of an investigational medicinal product (CTIMP)' it does not fall under The Medicines for Human Use (Clinical Trials) Regulations 2004. However, the research team will collect data on adverse events (AEs), serious adverse events (SAEs) or suspected unexpected serious adverse reactions (SUSARs) as defined by these regulations. Even in non-pharmaceutical research adverse incidents may still happen, for example:

- Minor injury
- breach of confidentiality
- patient complains about aspect of treatment as a trial participant
- deviation from trial protocol (e.g. randomising before consent)
- Aggressive behaviour of a participant towards the researcher, staff or others.

Participants are involved in the trial from the time consent has been given to when they have returned their follow-up measures to the research team. Serious adverse events must be reported to the research team within 24 hours and adverse events must be reported to the research team within 5 working days of the incident using an 'adverse incident report form'. Each incident will be followed through until it has been resolved. The Sponsor will be notified of these events and will advise on any further actions required.

Trial Steering Committee

A Trial Steering Committee consists of the CI, PI, two members of the research team, an independent Chair, and three other independent members, including a member of the PPI panel.

Furthermore, the entire Research Team (including all named investigators and collaborators of the NIHR Programme Grant) form a Programme Management Group which will oversee the running of the present trial (as part of the overall NIHR Programme grant that encompasses the present trial); the Group meets once a year in March-April.

Patient and Public Involvement

For the ongoing research programme, we have a lay advisory group of six PPI representatives. The PPI panel have read and approved the research proposal for this trial. They have provided feedback on the research question, what the research aims to achieve, the feasibility and acceptability of the research methods, and the dissemination and implementation plans. The advisory group have also been consulted on the design of information sheets and consent forms for participants, the intervention content and delivery, and undertaking the research (e.g., recruitment and retention) and will be consulted on the analysis and interpretation of the findings.

REC and R&D Approval

Before recruitment of participants commences at any CCG site, the following shall be sought

- [Primary Care RMG - Letter of Assurance](#)
- [Approval from the relevant NHS REC\(s\)](#)

- [GP Agreements](#)

as required under the NHS Research Governance Framework for Health and Social Care.

Any subsequent amendments to trial documentation, along with safety, annual progress and final trial reports will be submitted to R&D and REC for information and/or approval, as required.

All data will be processed in accordance with the Data Protection Act 1998.

Dissemination of Findings

Information on the progress of the VBI Trial will be publicly available via a number of organisations' websites including;

University of Cambridge PCU site: <http://tiny.cc/VBIprog>

UKCRN Portfolio: <http://public.ukcrn.org.uk/search/>

ISRCTN Register: <http://isrctn.org/>

Results of the research will be published in peer-reviewed journals and findings presented to a wide audience, including national and international conferences and other scientific meetings.

A lay summary of the results will be prepared and sent to all participants via a newsletter when available.

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